

Notice of Allowability

Application No.

10/614,266

Examiner

Hector M Reyes

Applicant(s)

YAHALOMI ET AL.

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4-19-2004.
2. ☒ The allowed claim(s) is/are 1-57.
3. ☒ The drawings filed on 19 April 2004 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 4/19/04
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

DETAILED ACTION

Status of the Claims

Currently claims 1-57 are under Examination.

Allowance

The following is an examiner's statement of reasons for allowance: Applicants claim a series of processes for preparing (-)-N-(trans-4-isopropylcyclohexanecarbonyl)-D-phenylalanine also known as nateglinide. Particularly, it is claim:

- In claims 1-6; 7-11; 56 and 57 processes wherein trans-4-isopropylcyclohexane carboxylic acid is reacted with **thionyl chloride** in presence of an **organic amide** in order to obtain trans-4-isopropylcyclohexane acid chloride, which is further use in the synthesis of nateglinide;
- In claims 12-33 a process requiring a **two phase system** wherein an alkaline earth or alkali metal salt of D-phenyl alanine in aqueous solution is reacted with trans-4-isopropylacid chloride dissolve in a water-immiscible solvent;
- In claims 34-48, a process requiring the preparation of an aqueous solution of an **alkaline earth metal salt of D-phenyl alanine in water free of a co-solvent** that is further reacted with trans-4-isopropylacid chloride as a neat reagent
- In claim 49-55, a process requiring a solution of a **tertiary amine salt of D-phenylalanine** combine with trans-4-isopropylcyclohexane carboxylic acid chloride in presence of an amide.

No prior art disclosing or suggesting processes outlined in claims 1-57. The closest art relevant to the instant invention was found in:

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- CA 123 :55430 for Toshihiro et al, JP 070177899 (1995) and
- Takahashi et al, WO 02/32854

Toshihiro discloses the preparation of nateglinide by reacting trans-4-

isopropylcyclohexanecarboxylic acid with phosphorus pentachloride in order to obtain trans-4-isopropylcyclohexanecarboxylic acid chloride, which is further reacted with phenylalanine.

Toshihiro discloses that the replacement of phosphorus pentachloride by thionyl chloride produce unwanted cis isomer of 4-isopropylcyclohexanecarboxylic acid chloride thus the said reference teaches away from the use of thionyl chloride, since it is the trans-4-isopropylcyclohexanecarboxylic acid chloride ~~the~~ isomer required for the preparation of the target compound. Thus, Toshihiro does not suggest the processes outlined in claims 1-6, 7-11, 56 and 57, which require the use of thionyl chloride.

On the other hand, Takahashi discloses the preparation of nateglinide by reacting trans-4-isopropylcyclohexanecarboxylic acid chloride with D-phenyl alanine in a mixed solvent consisting of a ketone and water in the presence of a base. However, Takahashi does not suggest:

- A two phase system as required in claims 12-33 or
- The preparation of an aqueous solution of an alkaline earth metal salt of D-phenyl alanine in water **free of a co-solvent** that is further reacted with trans-4-isopropylacid chloride as a neat reagent as required in claims 34-48 or
- A solution of a tertiary amine salt of D-phenylalanine combine with trans-4-isopropylcyclohexane carboxylic acid chloride in presence of an amide as required in the process described in claims 49-55.

CONCLUSION

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee.

Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

All post-Allowance Correspondence concerning this Application must be mailed to:

**BOX ISSUE FEE
COMMISSIONER FOR PATENTS
WASHINGTON, DC 20231**

Or you can fax them to the Office of Patent Publications at 703-308-5083, in order to expedite the handling of such correspondence as amendments under 37 CFR 1.312; information disclosure statements, and formal drawings. Sending Post-Allowance papers to Technology Center 1600 will only cause delays in matching papers with the case.

For information concerning status of correspondence sent after receipt of the Notice of Allowance, please contact the Correspondence Branch at (703) 305-8027.

Héctor M. Reyes, PhD JD
USPTO Reg. # P-54846
AU 1625
September 28, 2004

R. Desai
9/30/04